

B2 cont.
26. (new) A process for plant growth regulation which comprise applying an effective amount of the composition of claim 25 to plants or plant seeds.

REMARKS

The telephone election of example 11 is hereby affirmed. In the event that a further election of a process is required, group IV is elected.

In paragraph 7 of the Office Action, claims 1 and 2 were objected to on the ground that the word "naphthyl" was spelled incorrectly. These claims have been revised to correct the spelling error and a number of minor amendments have been made to correct punctuation and usage of language. For these reasons, it is requested that this ground of objection be withdrawn.

In paragraph 9 of the Office Action, claim 1 was rejected under 35 U.S.C. §112, first paragraph, because the specification does not reasonably provide enablement for the broad spectrum of substituents for radicals R_1 - R_6 in formula I is claim 1.

Reconsideration is requested.

The specification is directed to one who is skilled in the art and as such it does not have to recite that which is well known in the art. One who is skilled in this art can readily prepare the various compounds of claim 1 without the exercise of inventive faculty. The Examiner has not pointed to any particular compound which cannot be made based on the present specification and the skill of the art.

The claimed compounds may be made from the compounds of formula 2 which is set forth in claim 4. Compounds within the scope of formula 2 are well known and many are commercially available. For example, the compounds 2-oxo-1-cyclohexanepropionic acid; methyl-2-oxocyclohexanepropionate; 1-methyl-2-oxocyclohexanepropionic acid are all commercially available from Sigma Aldrich Chemical Company. Other compounds of formula 2 are commercially available or may be readily made

by a chemist with ordinary skill.

The Examiner has cited In re Wands, 8 USPQ2d 1400 (Fed. Cir. 1988) and In re Foreman, 230 USPQ 546 (Bd. of Pat. App. & Int. 1986) as support for the present rejection. Those cases held that the only issue is whether or not undue experimentation is required in connection with inventions involving a biological material which may have to be deposited with a culture collection. The level of skill in the art is such that it allows the making, without undue experimentation, of the intermediate compounds required for the practice of the present invention. The present specification contains 12 working examples and a flow sheet which describes how to make the compounds. It is not necessary that each compound with the genus be illustrated in order for the specification to be enabling. Each of the R₁-R₆ substituents are known and the Examiner has not pointed to any particular substituents as being unfamiliar to those who are skilled in the art. For these reasons, it is requested that this ground of rejection be withdrawn.

In paragraph 10 of the Office Action, claim 13 was rejected under 35 U.S.C. §112, first paragraph.

Reconsideration is requested.

Claim 13 has been canceled and is no longer at issue in the present application.

In paragraph 11 of the Office Action, claim 14 was rejected under 35 U.S.C. §112, first paragraph.

Reconsideration is requested.

Claim 14 has been rewritten to place in separate claims a method claim for each of the specified conditions. The specification has disclosed that the compounds of the invention inhibit the enzyme 5α-reductase. It is known that the inhibition of this enzyme has a favorable effect on each of the conditions that were listed in claim 14 as disclosed in the specification at page 2, lines 7-26. For these reasons, it is requested that the claimed methods are enabled

In paragraph 12 of the Office Action, claims 2 and

15 were rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention.

Reconsideration is requested.

The text of claim 2 has been revised to insert the definition for R and R'. Claim 15 has been canceled and new claim 24 has been drafted as a method of use claim which recites the step of applying the compounds. The term "heterocycle" as used in claims 1 and 2 is not indefinite. This term circumscribes a finite number of compounds which a skilled chemist can identify as being within the claims. For these reasons, it is requested that this ground of rejection be withdrawn.

In paragraph 13 of the Office Action, claims 1 and 10-12 were rejected under 35 U.S.C. §102(b) as being anticipated by CA 103:195974.

Reconsideration is requested.

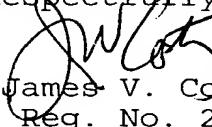
The CA 103:195974 reference is an Abstract of J. Chem. Research (S) 1985, 169, a copy of which is attached to this Amendment. This reference only discloses quinolizines where the unsaturated heterocycle group is unsubstituted. The claimed compounds all are substituted on the unsaturated ring as shown in claim 1. In addition, there is no X substituent as claimed by the applicant in the compounds of the cited reference. For these reasons there is no anticipation of the claims of the present application and it is requested that this ground of rejection be withdrawn.

The objection to claim 3 has been overcome by the revision of claim 1.

Authorization is given to charge any additional fee to Deposit Account No. 08-1540.

An early and favorable action is earnestly solicited.

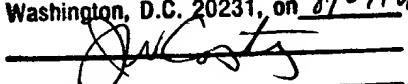
Respectfully submitted,


James V. Costigan
Reg. No. 25,669

MAILING ADDRESS:

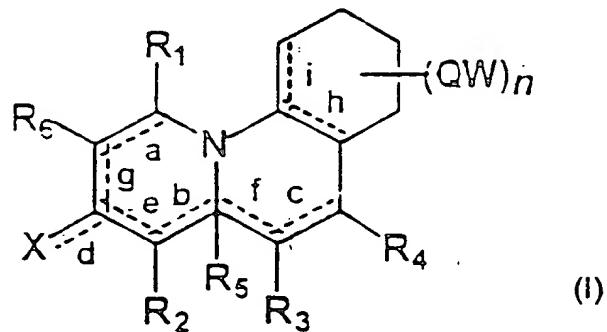
HEDMAN & COSTIGAN, P.C.
1185 Avenue of the Americas
New York, NY 10036-2601
(212) 302-8989

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Marked up copy of amended claims:

1. (amended) Fully and partially reduced benzo(c)quinolizine [benzo [c] -quinolizine] compounds of formula (1):



wherein:

R_1 , R_2 , R_3 , R_4 and R_6 , which are the same or different, are chosen from the group consisting of: H, C_{1-8} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, cyclopropane, cyclobutane, cyclopentane, cyclohexane, cycloheptane, cyclooctane, norbornane, canphane, adamantane, phenyl, biphenyl, naphthyl [naphtyl], saturated or aromatic heterocycle containing one or more N atoms, halogen, CN, azide, NRR' , C_{1-8} alkylamino, arylamino, C_{1-8} alkyloxy, aryloxy, $COOR$, $CONRR'$, $C(=O)R$, wherein R and R' , which are the same or different [from one another], are chosen [in] from the group consisting of H, C_{1-8} alkyl, cyclopropane, cyclobutane, cyclopentane, cyclohexane, cycloheptane, cyclooctane, norbornane, canphane, adamantane, phenyl, biphenyl, naphthyl [naphtyl], saturated or aromatic heterocycle containing one or more N atoms, [phenyl-, biphenyl-, naphthyl- C_{1-8} alkyl] naphthyl- C_{1-8} ;

R_5 is chosen [in] from the group consisting of: H, C_{1-8} alkyl, C_{1-8} alkyl-phenyl, [-biphenyl, [-naphtyl] naphthyl, COOR, CN, [,] phenyl, [biphenyl, napthyl,] saturated or aromatic heterocycle containing one or more N atoms, C_{1-8} alkyl-saturated or aromatic heterocycle containing one or more N atoms; C_{1-8} alkyl saturated or aromatic heterocycle containing one or more N atoms-ribose phosphate;

x is chosen from [in] the group consisting of: O, C(=O)R,

COOR, NO₂, and CONNR', wherein R and R' are as above defined; Q is chosen from [in] the group consisting of [simple] single-bond, C₁₋₈ alkyl, C₂₋₈ alkenyl, C₂₋₈ alkynyl, cyclopropane, cyclobutane, cyclopentane, cyclohexane, cycloheptane, cyclooctane, norbornane, canphane, adamantane, CO, CONR, and NR, where R is as above defined; W is chosen from [in] the group consisting of H, C₁₋₈ alkyl, C₂₋₈ alkenyl, C₂₋₈ alkynyl, cyclopropane, cyclobutane, cyclopentane, cyclohexane, cycloheptane, cyclooctane, norbornane, canphane, adamantane, trifluoromethyl, C₁₋₈ alkoxy, C₁₋₈ alkoxy-C₁₋₈ alkyl, phenyl [-], biphenyl [-], [naphthyl-C₁₋₈ alkyl] naphthyl-C₁₋₈ alkyl, phenyl, biphenyl, [naphthyl] naphthyl, phenoxy, biphenyloxy, [naphthoxy] naphthoxy, phenylamino, biphenylamino, [naphylamino] naphthylamino, C₁₋₈ alkyl-carbonyl, phenylcarbonyl, biphenylcarbonyl, [naphylcarbonyl] naphthylcarbonyl, phenylcarboxyl, biphenylcarboxyl, [naphylcarboxyl] naphthylcarboxyl, phenylcarboxyamide, biphenylcarboxyamide, [naphylcarboxyamide] naphthylcarboxyamide, halogen, CN, NRR', C₁₋₈ alkylamino, saturated or aromatic heterocycle containing one or more N atoms wherein the groups alkyl, alkenyl, alkynyl, cyclopropane, cyclobutane, cyclopentane, cyclohexane, cycloheptane, cyclooctane, norbornane, canphane, adamantane, phenyl, biphenyl, naphthyl [naphyl], saturated or aromatic heterocycle containing one or more N atoms, can be substituted; n is an integer comprised between 1 and 4; the symbol ----- means that the corresponding bonds a, b, c, d, e, f, g, h and i [can be a simple] are single or double bonds, with the proviso that when b or f are a double bond, the group R₅ is absent; their pharmaceutically acceptable salts and esters.

2. (amended) [Benzo[c]quinolizine] Benzo(c)quinolizine compounds of formula (1) according to Claim 1, wherein R₅ = h, C₁₋₈ alkyl-phenyl, biphenyl, [-naphthyl] naphthyl, saturated or aromatic heterocycle containing one or more N atoms, C₁₋₈

alkyl-saturated or aromatic heterocycle containing one or more N atoms; or a [group] C_{1-8} alkyl-saturated or aromatic heterocycle containing one or more N atoms-ribose-phosphate.;
 $X = O, COOH$;

$Q =$ [simple] single bond, CO, CONR, NR_2 [() wherein R is as above defined)], wherein R is chosen from the group consisting of H, C_{1-8} alkyl, cyclopropane, cyclobutane, cyclopentane, cyclohexane, cycloheptane, cyclooctane, norbornane, canphane, adamantane, phenyl, biphenyl, naphthyl, saturated or aromatic heterocycle containing one or more N atoms, naphthyl- C_{1-8} alkyl;

$W =$ H, F, Cl, Br, Me, t-butyl, C_{1-8} alkoxy, 2,5-dimethylhexyl, trifluoromethyl, 2,5-(di-trifluoromethyl)-phenyl, 4-methyloxy-phenyl, phenyl, phenyl- C_{1-8} alkyl, C_{1-8} alkylcarbonyl, phenylcarbonyl[.];

$n = 1$ and 2;

R_1, R_2, R_3, R_4 and $R_6 =$ H, Me, CN, phenyl, COOR, CONRR', $C(=O)R$, [() wherein R and R' [are as above defined)], are the same or different and are chosen from the group consisting of H, C_{1-8} alkyl, cyclopropane, cyclobutane, cyclopentane, cyclohexane, cycloheptane, cyclooctane, norbornane, canphane, adamantane, phenyl, biphenyl, naphthyl, saturated or unsaturated heterocycle containing one or more N atoms, naphthyl- C_{1-8} .

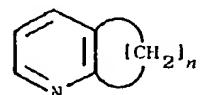
Addition Reactions of Heterocyclic Compounds. Part 81.¹
Products from Dimethyl Acetylenedicarboxylate with Some
Cycloalkyl[*b*]pyridines

J. Chem. Research (S),
 1985, 169
J. Chem. Research (M),
 1985, 1901-1915

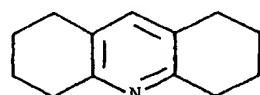
PATRICK J. ABBOTT, R. MORRIN ACHESON,* and MICHAEL C. K. CHOI

Department of Biochemistry, South Parks Road, Oxford OX1 3QU, U.K.

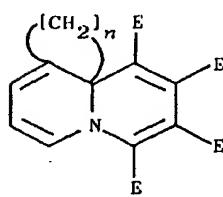
The reaction of dimethyl acetylenedicarboxylate (DMAD) with five cycloalkyl[*b*]pyridines to give tetramethyl 9a*H*-quinolizine-1,2,3,4-tetracarboxylates, along with other quinolizines and oxoquinolizines which were identified from their spectra, is described.



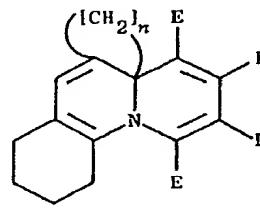
(1) $n = 3$
 (2) $n = 4$
 (3) $n = 5$
 (4) $n = 10$



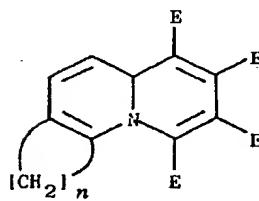
(5)



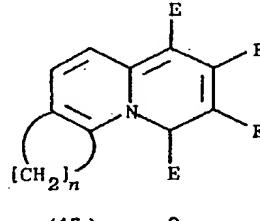
(6) $n = 3$
 (7) $n = 4$
 (8) $n = 5$
 (9) $n = 10$



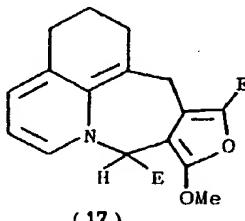
(10)



(12) $n = 4$
 (13) $n = 5$
 (14) $n = 10$



(15) $n = 3$
 (16) $n = 10$



E = CO₂Me

In view of the wide structural variety of products which are formed from DMAD and 2-methylpyridines,^{2,3} and from strained and unstrained indoles possessing 2,3-polymethylene bridges,⁴ the reactions of DMAD with the pyridine derivatives (1)-(5) were investigated. In all cases the major products were the quinolizines (6)-(10) and (12)-(15) respectively. A minor product from (2) was provisionally formulated as (17). It was noteworthy that the pyridine (4) gave mainly the 9a*H*-quinolizine (14), rather than the 9a-alkyl-9a*H*-quinolizine (9) and that the 9a*H*-isomer (14) required an unusually high temperature to effect the normally ready thermal [1,5] sigmatropic shift⁵ to the 4*H*-isomer (16).

The quinolizines were all identified from the similarity of their spectra, particularly their u.v. and ¹H n.m.r. spectra, to those of other quinolizines.

We thank Dr. R. T. Aplin for the mass spectra and the Croucher Foundation for a Post-doctoral Fellowship (to M.C.K.C.).

Techniques used: I.r., u.v., n.m.r., mass spectrometry

References: 12

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References cited in this synopsis:

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*To receive any correspondence.